REMARKS

Status of the Claims

Pending claims

Claims 1 to 17 and 28 to 38 are pending (claims 18 to 27 were canceled in the preliminary amendment).

Claims added and amended in the instant amendment

Claims 1 to 6, 8 to 17, 31 to 33 and 37 are amended, and claims 39 to 44 are added. Thus, after entry of the instant amendment, claims 1 to 17 and 28 to 44 will be pending.

Claims 34, 35 and 38 were withdrawn, thus, claims 1 to 17 and 28 to 33, 36, 37, and 39 to 44 will be pending and under consideration.

Outstanding Rejections

Claims 3, 4 to 6, 31, 32 and 37 stand rejected under 35 U.S.C. §112, second paragraph. Claims 4 to 6, 7 to 11 and 12 to 17, are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification. Claims 1 to 3, 4 to 6, 7 to 11, 12 to 17, 28 to 33, 36 and 37 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. Claims 4 to 6, 7 to 11 and 12 to 17 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Gelfand, et al., U.S. Patent No. 5,491,086, issued February 13, 1996. Claims 1 to 17, 28 to 33, 36 and 37 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1 to 30 of U.S. Patent No. 5,948,666. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to nucleic acids having a sequence with at least about 97%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, or at least 50% homology to an exemplary nucleic acid of the invention and fragments comprising at least about 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases thereof, and the sequences complementary thereto, can

be found, inter alia, in the paragraph spanning pages 42 and 43, and lines 9 to 15 of page 43. Support for claims directed to methods for producing a biologically active polypeptide and screening the polypeptide for enhanced activity can be found, inter alia, on line 30, page 26 to line 9, page 31. Support for claims directed to polymerases having activity in various salinity conditions can be found, inter alia, on page 70, lines 5 to 9.

The restriction requirements and election

In the restriction requirement of March 25, 2003, the Patent Office alleged that the pending claims of the application are directed to three separate and distinct inventions under 35 U.S.C. §121:

Group I, claims 1 to 17, drawn to an isolated nucleic acid encoding a polymerase;

Group II, claims 18 to 26, drawn to an isolated DNA polymerase;

Group III, claim 27, drawn to an assay for identifying functional polypeptides.

In response to the Restriction Requirement, Applicants elected Group I, claims 1 to 17, drawn to an isolated nucleic acid encoding a polymerase.

In the instant office action of August 20, 2003, claims 34, 35 and 38 were withdrawn as allegedly being drawn to a non-elected invention. Applicants respectfully request that, after the elected product claims have been found to be allowable, all withdrawn process (methods) claims which depend from or otherwise include all of the limitations of the allowed product claims be rejoined. MPEP §821.04; pg 800-63, 8th Edition, Aug. 2001/ revision Feb. 2003; In re Ochiai, 37 USPQ2d 1127 (Fed. Cir. 1995); In re Brouwer, 37 USPQ2d 1663 (Fed. Cir. 1995); 1184 OG 86, 3/26/96.

Amendment to claim 2

The Office Action noted that the amendment to claim 2 in the preliminary amendment was not entered. Accordingly, the instant amendment to claim 2 is based on claim 2 as filed.

Priority

The specification has been amended to reflect that priority document USSN 09/391,340, has issued as U.S. Patent No. 6,492,511 B2.

Information Disclosure Statements

Applicants thank the Examiner for expressly considering (and initialing) the Information Disclosure Statements (IDSs) and Forms PTO-1449, submitted October 2, 2002, and February 4, 2003.

Claim objections

The objections to claims 1 and 37 have been addressed in the instant amendment.

Issues under 35 U.S.C. §112, second paragraph

Claims 3, 4 to 6, 31, 32 and 37 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The phrase "sequences complementary thereto"

Claims 3 and 12 are alleged to be indefinite because of the phrase "sequences complementary thereto." The instant amendment addresses this issue.

The terms "high stringency", "moderate stringency" and "low stringency"

The Patent Office alleged claims 4 to 6 are indefinite because of the terms "high stringency", "moderate stringency" and "low stringency". The instant amendment addresses this issue. The terms have been deleted and replaced by specific hybridization conditions.

The phrase "high salinity conditions"

The Patent Office alleged claim 33 is indefinite because of the term "high salinity conditions". The instant amendment addresses this issue. The term has been deleted and replaced by specific conditions.

Claims 31, 32 and 37

The instant amendment addresses the objections to claims 31, 32 and 37.

Issues under 35 U.S.C. §112, first paragraph

Written Description

Claims 4 to 6, 7 to 11 and 12 to 17, are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such as

way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, the Patent Office alleged, inter alia, that the claimed genus of polynucleotides is not disclosed in the specification because it is a large variable genus, and that a single species of the claimed genus is insufficient to put one of skill in the art in possession of all of the attributes and features of all species in the claimed genus.

Applicants respectfully submit that the claimed invention is sufficiently described in the specification such that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing. Applicants respectfully aver that a single species of a genus can be sufficient to put one of skill on the art in possession of all species with a claimed genus.

Applicants respectfully submit that only structurally and functionally related nucleic acids are encompassed by the scope of the claims. The nucleic acids of the claimed invention are described by structure (the exemplary sequences), a physico-chemical property (percent sequence identity and/or hybridization conditions) and function (polymerase activity). All nucleic acids of the claimed genus must encode an enzyme having a percent sequence identity to an exemplary polymerase coding sequence, or, hybridize under specific conditions to an exemplary polymerase coding sequence. Applicants respectfully submit that describing a genus of polynucleotides in terms of physico-chemical properties (e.g., sequence identity or hybridization conditions) and function (e.g., encoding polypeptides having polymerase activity) satisfies the written description requirement of section 112, first paragraph.

The Patent Office alleged that a single species of a genus is insufficient to put one of skill on the art in possession of all species within a claimed genus. However, Applicants respectfully aver that even a single species of the instant invention is sufficient to put one of skill on the art in possession of the claimed genus. There is no bright line rule that a single species of a genus is insufficient to put one of skill on the art in possession of all species with a claimed genus. Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph. In example 14 of the guidelines (a copy of which is attached as Exhibit A), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that

are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogously, the genus of nucleic acids of the claimed invention is described by structure (the exemplary nucleic acids or polypeptide sequences), a physico-chemical property (percent sequence identity or stringent hybridization conditions) and function (having an polymerase activity). All nucleic acids of the genus used in the claimed methods must have a percent sequence identity to an exemplary sequence of the invention (or, hybridize under specific conditions to an exemplary sequence of the invention). The USPTO guidelines recognize that written description is met for a genus of polypeptides described by structure, a physico-chemical property (e.g., a % sequence identity, hybridization under specific conditions) and a defined function (e.g., polymerase activity), the genus of claimed polypeptides also meet the written description requirements of section 112.

The genus of nucleic acids of the claimed invention also fully comply with the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997). In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) Lilly, 43USPQ2d at 1406.

As noted above, the instant claims clearly set forth specific structural and physical characteristics of the claimed polymerase-encoding nucleic acids. The claimed genus of polypeptides all must have polymerase activity and a specific physical characteristic, e.g., a % sequence identity to the exemplary nucleic acid, or, hybridization under specific conditions to an

exemplary sequence of the invention. Therefore, the genus of nucleic acids used in the claimed methods is defined via shared physical and structural properties in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

More recently, the Federal Circuit stated

Similarly, in this court's most recent pronouncement, it noted:

> More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the function of the esterases encoded by the nucleic acids of the invention is sufficiently correlated to a particular, known structure (the exemplary sequences) and a physical (physico-chemical) property (percent sequence identity or specific hybridization conditions). Accordingly, the sequences used in the claimed methods are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Applicants also respectfully refer to recently issued claims directed to genuses of polynucleotides based on sequence identity (and stringent hybridization) to an exemplary nucleic acid, see, e.g., recently issued claims directed to, e.g., 72.5% sequence identity, as in USPN 6,593,514; 75% sequence identity, as in USPN 6,586,215; 80% sequence identity, as in USPN 6,596,926; 85% sequence identity, as in USPN 6,590,141 and USPN 6,586,179; 86% sequence identity, as in USPN 6,583,337; 90% sequence identity (and "stringent hybridization"), as in USPN 6,541,684 (see Exhibit B).

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described

in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Enablement

Claims 1 to 3, 4 to 6, 7 to 11, 12 to 17, 28 to 33, 36 and 37 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention.

The Patent Office states that the specification is enabling for the polynucleotide of SEQ ID NO:1 which encoding a polypeptide having polymerase activity.

However, it is alleged, inter alia, that the specification does not provide reasonable enablement for the large number of claimed polymerase-encoding polynucleotides. The Patent Office alleged that it is not routine experimentation to screen for multiple substitutions or multiple modifications as encompassed by the claims. It is alleged that it would have required some knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with polymerase activity to create variants of an exemplary nucleic acid and test them for the expression of polypeptides having polymerase activity.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of polymerases to practice the claimed invention. As declared by Dr. Jay Short (see attached Rule 132 declaration), the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for various polymerase activities (e.g., thermostable DNA polymerase activity), was very high. As declared by Dr. Short, using the teaching of the specification, one skilled in the art could have selected routine methods known in the art at the time of the invention to express variants of nucleic acids encoding the exemplary enzyme of the invention and screen them for expression of polypeptides having various polymerase activities. Dr. Short declares that one skilled in the art could have used routine protocols known in the art at the time of the invention, including those described in the instant specification, to screen for nucleic acids encoding polypeptides having a percent sequence identity to SEQ ID NO:1, or active fragments thereof, for various polymerase activities. Dr. Short declares that it was routine to screen for multiple substitutions or multiple modifications of an enzyme-encoding sequence and predictably achieve positive results. As declared by Dr. Short, while the numbers of samples needed to be screened may have been high,

the screening procedures were routine and successful results (i.e., finding variant nucleic acids encoding polymerases having various activties) predictable.

Furthermore, Dr. Short declares that it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with polymerase activity to create variants of the exemplary nucleic acid and test them for the expression of polypeptides or peptides having polymerase activity. Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including identification of a genus of nucleic acids encoding polymerases active under various conditions.

Whether large numbers of compositions (e.g., enzymes, antibodies, nucleic acids, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in In re Wands directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also recognize the need to screen numbers of negatives to find a sample that has the desired

properties, e.g., polymerase-encoding activity. Furthermore, as declared by Dr. Short, the screening procedures used to identify nucleic acids within the scope of the instant invention (e.g., identifying nucleic acids encoding polymerase active under various conditions) were all well known in the art and at the time this application was filed. All were routine protocols for the skilled artisan. Thus, the skilled artisan using Applicants' written disclosure could practice the instant claimed invention without undue experimentation.

Accordingly, Applicants respectfully submit that the pending claims meet the written description and enablement requirements under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §102

Gelfand, et al., U.S. Patent No. 5,491,086

Claims 4 to 6, 7 to 11 and 12 to 17 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Gelfand, et al., U.S. Patent No. 5,491,086, issued February 13, 1996. It is alleged that Gelfand, et al., teaches a nucleic acid 66.5% identical to the instantly disclosed SEQ ID NO:1, and, the DNA taught by Gelfand, et al., comprises many regions of at least 10 consecutive bases of a sequence as set forth in SEQ ID NO:1 and encodes a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO:2. It is further alleged that Gelfand, et al., anticipates claims 4 to 6, drawn to a nucleic acids that hybridize to a nucleic acid of the invention under conditions of high to low stringency.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention.

Applicants respectfully submit that the instant amendment addresses these issues. After entry of the instant amendment, the claims are drawn to nucleic acids hybridizing under specific hybridization conditions, wherein the claimed nucleic acids will not hybridize to a nucleic acid 66.5% identical to the instantly disclosed SEQ ID NO:1, i.e., the nucleic acid of Gelfand, et al. Also after entry of the instant amendment, the claims are drawn to nucleic acids comprising at least 20 consecutive bases of a sequence as set forth in SEQ ID NO:1 or at least 20

consecutive bases of a sequence having at least 70% identity to SEQ ID NO:1 and encoding a polypeptide having a polymerase activity. Thus, the rejection under section 102(b) can be properly withdrawn.

Issues regarding Double Patenting

Claims 1 to 17, 28 to 33, 36 and 37 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1 to 30 of U.S. Patent No. 5,948,666. A terminal disclaimer under 37 CFR §§3.73(b) and 1.321(b) addressing this issue is attached. Accordingly, the rejection under the judicially created doctrine of obviousness-type double patenting can be withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs, 35 U.S.C. §102(b), and the judicially created doctrine of obviousness-type double patenting. Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952. Please credit any overpayment to this account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 720-5133.

Respectfully submitted,

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Gregory P. Einhorn
Reg. No. 38,440
Morrison & Foerster LLP
3811 Valley Centre Drive, Suite 500
San Diego CA 92130-2332
Tel: 858-720-5133
Fax: 858-720-5125